

## General

### Guideline Title

Intravenous fluid therapy in adults in hospital.

### Bibliographic Source(s)

National Clinical Guideline Centre. Intravenous fluid therapy in adults in hospital. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Dec. 36 p. (Clinical guideline; no. 174).

### Guideline Status

This is the current release of the guideline.

## Recommendations

### Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

#### Principles and Protocols for Intravenous (IV) Fluid Therapy

The assessment and management of patients' fluid and electrolyte needs is fundamental to good patient care.

Assess and manage patients' fluid and electrolyte needs as part of every ward review. Provide IV fluid therapy only for patients whose needs cannot be met by oral or enteral routes, and stop as soon as possible.

Skilled and competent healthcare professionals should prescribe and administer IV fluids, and assess and monitor patients receiving IV fluids.

When prescribing IV fluids, remember the 5 Rs: Resuscitation, Routine maintenance, Replacement, Redistribution and Reassessment.

Offer IV fluid therapy as part of a protocol (see the following algorithms for IV fluid therapy in the full version of the guideline document [see the "Availability of Companion Documents" field]):

- Assess patients' fluid and electrolyte needs following Algorithm 1: Assessment.
- If patients need IV fluids for fluid resuscitation, follow Algorithm 2: Fluid resuscitation.
- If patients need IV fluids for routine maintenance, follow Algorithm 3: Routine maintenance.
- If patients need IV fluids to address existing deficits or excesses, ongoing abnormal losses or abnormal fluid distribution, follow Algorithm 4: Replacement and redistribution.

Include the following information in IV fluid prescriptions:

- The type of fluid to be administered
- The rate and volume of fluid to be administered

Patients should have an IV fluid management plan, which should include details of:

- The fluid and electrolyte prescription over the next 24 hours
- The assessment and monitoring plan

Initially, the IV fluid management plan should be reviewed by an expert daily. IV fluid management plans for patients on longer-term IV fluid therapy whose condition is stable may be reviewed less frequently.

When prescribing IV fluids and electrolytes, take into account all other sources of fluid and electrolyte intake, including any oral or enteral intake, and intake from drugs, IV nutrition, blood and blood products.

Patients have a valuable contribution to make to their fluid balance. If a patient needs IV fluids, explain the decision, and discuss the signs and symptoms they need to look out for if their fluid balance needs adjusting. If possible or when asked, provide written information (for example, NICE's Information for the public [see the "Patient Resources" field]), and involve the patient's family members or carers (as appropriate).

### Assessment and Monitoring

#### Initial Assessment

Assess whether the patient is hypovolaemic. Indicators that a patient may need urgent fluid resuscitation include:

- Systolic blood pressure is less than 100 mmHg
- Heart rate is more than 90 beats per minute
- Capillary refill time is more than 2 seconds or peripheries are cold to touch
- Respiratory rate is more than 20 breaths per minute
- National Early Warning Score (NEWS) is 5 or more
- Passive leg raising suggests fluid responsiveness<sup>1</sup>

<sup>1</sup>Passive leg raising is a bedside method to assess fluid responsiveness in a patient. It is best undertaken with the patient initially semi-recumbent and then tilting the entire bed through 45°. Alternatively it can be done by lying the patient flat and passively raising their legs to greater than 45°. If, at 30–90 seconds, the patient shows signs of haemodynamic improvement, it indicates that volume replacement may be required. If the condition of the patient deteriorates, in particular breathlessness, it indicates that the patient may be fluid overloaded.

Assess the patient's likely fluid and electrolyte needs from their history, clinical examination, current medications, clinical monitoring and laboratory investigations:

- History should include any previous limited intake, thirst, the quantity and composition of abnormal losses (see "Diagram of Ongoing Losses" in the full version of the guideline document), and any comorbidities, including patients who are malnourished and at risk of refeeding syndrome (see [Nutrition support in adults](#) [NICE clinical guideline 32]).
- Clinical examination should include an assessment of the patient's fluid status, including:
  - Pulse, blood pressure, capillary refill and jugular venous pressure
  - Presence of pulmonary or peripheral oedema
  - Presence of postural hypotension
- Clinical monitoring should include current status and trends in:
  - NEWS
  - Fluid balance charts
  - Weight
- Laboratory investigations should include current status and trends in:
  - Full blood count
  - Urea, creatinine and electrolytes

#### Reassessment

If patients are receiving IV fluids for resuscitation, reassess the patient using the ABCDE approach (Airway, Breathing, Circulation, Disability, Exposure), monitor their respiratory rate, pulse, blood pressure and perfusion continuously, and measure their venous lactate levels and/or arterial pH and base excess according to guidance on advanced life support (Resuscitation Council [UK], 2011).

All patients continuing to receive IV fluids need regular monitoring. This should initially include at least daily reassessments of clinical fluid status, laboratory values (urea, creatinine and electrolytes) and fluid balance charts, along with weight measurement twice weekly. Be aware that:

- Patients receiving IV fluid therapy to address replacement or redistribution problems may need more frequent monitoring.
- Additional monitoring of urinary sodium may be helpful in patients with high-volume gastrointestinal losses. (Reduced urinary sodium excretion [less than 30 mmol/l] may indicate total body sodium depletion even if plasma sodium levels are normal. Urinary sodium may also indicate the cause of hyponatraemia, and guide the achievement of a negative sodium balance in patients with oedema. However, urinary sodium values may be misleading in the presence of renal impairment or diuretic therapy.)
- Patients on longer-term IV fluid therapy whose condition is stable may be monitored less frequently, although decisions to reduce monitoring frequency should be detailed in their IV fluid management plan.

If patients have received IV fluids containing chloride concentrations greater than 120 mmol/l (for example, sodium chloride 0.9%), monitor their serum chloride concentration daily. If patients develop hyperchloraemia or acidaemia, reassess their IV fluid prescription and assess their acid–base status. Consider less frequent monitoring for patients who are stable.

Clear incidents of fluid mismanagement (for example, unnecessarily prolonged dehydration or inadvertent fluid overload due to IV fluid therapy) should be reported through standard critical incident reporting to encourage improved training and practice (see "Consequences of fluid mismanagement to be reported as critical incidents" below).

If patients are transferred to a different location, reassess their fluid status and IV fluid management plan on arrival in the new setting.

### Resuscitation

If patients need IV fluid resuscitation, use crystalloids that contain sodium in the range 130–154 mmol/l, with a bolus of 500 ml over less than 15 minutes. (For more information, see the "Composition of commonly used crystalloids" table in the original guideline document.)

Do not use tetrastarch for fluid resuscitation.

Consider human albumin solution 4% to 5% for fluid resuscitation only in patients with severe sepsis.

### Routine Maintenance

If patients need IV fluids for routine maintenance alone, restrict the initial prescription to:

- 25–30 ml/kg/day of water and
- Approximately 1 mmol/kg/day of potassium, sodium and chloride and
- Approximately 50–100 g/day of glucose to limit starvation ketosis. (This quantity will not address patients' nutritional needs; see the NICE guideline [Nutrition support in adults](#) [NICE clinical guideline 32]).

For more information see "IV fluid prescription for routine maintenance over a 24-hour period" in the original guideline document.

For patients who are obese, adjust the IV fluid prescription to their ideal body weight. Use lower range volumes per kg (patients rarely need more than a total of 3 litres of fluid per day) and seek expert help if their BMI is more than 40 kg/m<sup>2</sup>.

Consider prescribing less fluid (for example, 20–25 ml/kg/day fluid) for patients who:

- Are older or frail
- Have renal impairment or cardiac failure
- Are malnourished and at risk of refeeding syndrome (see the NICE guideline [Nutrition support in adults](#) [NICE clinical guideline 32]).

When prescribing for routine maintenance alone, consider using 25–30 ml/kg/ day sodium chloride 0.18% in 4% glucose with 27 mmol/l potassium on day 1 (there are other regimens to achieve this). Prescribing more than 2.5 litres per day increases the risk of hyponatraemia. These are initial prescriptions and further prescriptions should be guided by monitoring.

Consider delivering IV fluids for routine maintenance during daytime hours to promote sleep and wellbeing.

### Replacement and Redistribution

Adjust the IV prescription (add to or subtract from maintenance needs) to account for existing fluid and/or electrolyte deficits or excesses, ongoing losses (see "Diagram of ongoing losses" in the original guideline document) or abnormal distribution.

Seek expert help if patients have a complex fluid and/or electrolyte redistribution issue or imbalance, or significant comorbidity, for example:

- Gross oedema
- Severe sepsis
- Hyponatraemia or hypernatraemia
- Renal, liver and/or cardiac impairment
- Post-operative fluid retention and redistribution
- Malnourished and refeeding issues

### Training and Education

Hospitals should establish systems to ensure that all healthcare professionals involved in prescribing and delivering IV fluid therapy are trained on the principles covered in this guideline, and are then formally assessed and reassessed at regular intervals to demonstrate competence in:

- Understanding the physiology of fluid and electrolyte balance in patients with normal physiology and during illness
- Assessing patients' fluid and electrolyte needs (the 5 Rs: Resuscitation, Routine maintenance, Replacement, Redistribution and Reassessment)
- Assessing the risks, benefits and harms of IV fluids
- Prescribing and administering IV fluids
- Monitoring the patient response
- Evaluating and documenting changes and
- Taking appropriate action as required

Healthcare professionals should receive training and education about, and be competent in, recognising, assessing and preventing consequences of mismanaged IV fluid therapy, including:

- Pulmonary oedema
- Peripheral oedema
- Volume depletion and shock

Hospitals should have an IV fluids lead, responsible for training, clinical governance, audit and review of IV fluid prescribing and patient outcomes.

"Diagram of ongoing losses" is available in the full version of the original guideline document.

### Consequences of Fluid Mismanagement to Be Reported as Critical Incidents

Consequence of Fluid Mismanagement	Identifying Features	Time Frame of Identification
Hypovolaemia	<ul style="list-style-type: none"> <li>• Patient's fluid needs not met by oral, enteral or IV intake and</li> <li>• Features of dehydration on clinical examination</li> <li>• Low urine output or concentrated urine</li> <li>• Biochemical indicators, such as more than 50% increase in urea or creatinine with no other identifiable cause</li> </ul>	Before and during IV fluid therapy
Pulmonary oedema (breathlessness during infusion)	<ul style="list-style-type: none"> <li>• No other obvious cause identified (for example, pneumonia, pulmonary embolus or asthma)</li> <li>• Features of pulmonary oedema on clinical examination</li> <li>• Features of pulmonary oedema on X-ray</li> </ul>	During IV fluid therapy or within 6 hours of stopping IV fluids
Hyponatraemia	<ul style="list-style-type: none"> <li>• Serum sodium less than 130 mmol/l</li> <li>• No other likely cause of hyponatraemia identified</li> </ul>	During IV fluid therapy or within 24 hours of stopping IV fluids
Hypernatraemia	<ul style="list-style-type: none"> <li>• Serum sodium 155 mmol/l or more</li> <li>• Baseline sodium normal or low</li> <li>• IV fluid regimen included 0.9% sodium chloride</li> <li>• No other likely cause of hypernatraemia identified</li> </ul>	During IV fluid therapy or within 24 hours of stopping IV fluids
Peripheral oedema	<ul style="list-style-type: none"> <li>• Pitting oedema in extremities and/or lumbar sacral area</li> <li>• No other obvious cause identified (for example, nephrotic</li> </ul>	During IV fluid therapy or within 24 hours of stopping IV fluids

Consequence of Fluid Mismanagement	Identifying Features (syndrome or known cardiac failure)	Time Frame of Identification
Hyperkalaemia	<ul style="list-style-type: none"> <li>Serum potassium more than 5.5 mmol/l</li> <li>No other obvious cause identified</li> </ul>	During IV fluid therapy or within 24 hours of stopping IV fluids
Hypokalaemia	<ul style="list-style-type: none"> <li>Serum potassium less than 3.0 mmol/l likely to be due to infusion of fluids without adequate potassium provision</li> <li>No other obvious cause (for example, potassium-wasting diuretics, refeeding syndrome)</li> </ul>	During IV fluid therapy or within 24 hours of stopping IV fluids

This table was drafted based on the consensus decision of the members of the Guideline Development Group.

See the original guideline document for the table 'IV Fluid Prescription (by body weight) for Routine Maintenance Over a 24-hour Period'.

## Clinical Algorithm(s)

An algorithm titled "Algorithms for IV Fluid Therapy" is provided in the full version of the original guideline document.

In addition, a NICE pathway on intravenous fluid therapy in adults in hospital is available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) .

## Scope

### Disease/Condition(s)

Any condition requiring intravenous (IV) fluids

### Guideline Category

Evaluation

Management

Treatment

### Clinical Specialty

Cardiology

Endocrinology

Geriatrics

Internal Medicine

Nursing

Nutrition

Pulmonary Medicine

Surgery

# Intended Users

Advanced Practice Nurses

Hospitals

Nurses

Physician Assistants

Physicians

## Guideline Objective(s)

- To provide guidance on intravenous (IV) fluid therapy for general areas of hospital practice, covering both the prescription and monitoring of IV fluid and electrolyte therapy, and the training and educational needs of all hospital staff involved in IV fluid management
- To help prescribers understand the:
  - Physiological principles that underpin fluid prescribing
  - Pathophysiological changes that affect fluid balance in disease states
  - Indications for IV fluid therapy
  - Reasons for the choice of the various fluids available
  - Principles of assessing fluid balance

Note: The scope of the guideline does not cover the practical aspects of administration (as opposed to the prescription) of IV fluids.

## Target Population

Adult hospital inpatients who require intravenous (IV) fluid therapy to prevent or correct problems with their fluid and/or electrolyte status

Note: The recommendations do not apply to patients under 16 years, pregnant women, and those with severe liver or renal disease, diabetes or burns. They also do not apply to patients needing inotropes and those on intensive monitoring and so they have less relevance to intensive care settings and patients during surgical anaesthesia. Patients with traumatic brain injury (including patients needing neurosurgery) are also excluded.

## Interventions and Practices Considered

1. Assessment of patient for hypovolaemia
2. Clinical examination (assessment of patient's fluid status, pulse, blood pressure, capillary refill and jugular venous pressure presence of pulmonary or peripheral edema, presence of postural hypotension)
3. Clinical monitoring (National Early Warning Score [NEWS], fluid balance charts, weight)
4. Laboratory investigations (full blood count, urea, creatinine and electrolytes)
5. Establishment of intravenous (IV) fluid management plan
6. Reassessment using the ABCDE approach (Airway, Breathing, Circulation, Disability, Exposure)
7. Monitoring of respiratory rate, pulse, blood pressure and perfusion continuously, and measurement of venous lactate levels and/or arterial pH
8. Daily reassessments of clinical fluid status (laboratory values including urea, creatinine and electrolytes, fluid balance charts, along with weight measurement twice weekly)
9. Reassessment of fluid status and IV fluid management plan on arrival in the new setting in patients who are transferred
10. IV fluid resuscitation
11. Routine maintenance: adjustment of fluids for specific patient populations
  - Obese patients
  - Old and frail
  - Impairment or cardiac failure
  - Malnourished patients at risk of refeeding syndrome
12. Delivery of IV fluids for routine maintenance during daytime hours to promote sleep and wellbeing
13. Replacement and redistribution
  - Prescription adjustment

- Consultation of expert help if patients have a complex fluid and/or electrolyte redistribution issue or imbalance, or significant comorbidity

#### 14. Healthcare professional education and training

## Major Outcomes Considered

- All-cause mortality within 30 days of hospitalization
- Length of stay in hospital
- Length of stay in Intensive care unit
- Quality of life
- Renal complications/acute kidney injury (AKI) defined as an increase of 50% or more of serum creatinine from baseline
- Respiratory complications including pulmonary oedema, respiratory failure, chest infection, mechanical ventilation
- Morbidity – measured by Sequential Organ Failure Assessment (SOFA) and Multiple Organ Dysfunction Score (MODS)
- Total volume of fluid received
- Hyperchloraemia
- Hyperchloraemic acidosis
- Hypochloraemia

## Methodology

### Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

### Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

#### Developing the Review Questions and Outcomes

Review questions were developed in a PICO framework (patient, intervention, comparison and outcome) for intervention reviews. This was to guide the literature searching process and to facilitate the development of recommendations by the Guideline Development Group (GDG). These were drafted by the NCGC technical team and refined and validated by the GDG. The questions were based on the key clinical areas identified in the scope (see Appendix A in the full version of the original guideline document). Due to the breadth of the scope and the target population, the GDG often found that several review questions could be generated for a single area within the scope. However, only 15 to 20 questions can be reasonably managed within the usual time frame of full clinical guideline development (18 months). Since it was not possible to cover all potentially important aspects, the GDG considered the relative importance of these and prioritised areas for developing review questions. This decision to prioritise certain areas took into consideration factors such as whether the area is a key clinical issue for the National Health Service (NHS), patient safety, cost (to the NHS), equality and variations in practice.

#### Searching for Evidence

##### Clinical Literature Search

Systematic literature searches were undertaken to identify evidence within published literature in order to answer the review questions as per The Guidelines Manual (2009). Clinical databases were searched using relevant medical subject headings, free-text terms and study type filters where appropriate. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English language. All searches were conducted on core databases, MEDLINE, EMBASE and The Cochrane Library. Additional subject specific

databases were used for some questions: CINAHL for questions on training and education, algorithms, urine output, and daily weights; PsycINFO for the training and education question. All searches were updated on 12 March 2013. No papers after this date were considered.

Search strategies were checked by looking at reference lists of relevant key papers, checking search strategies in other systematic reviews and asking the Guideline Development Group (GDG) for known studies. The questions, the study types applied, the databases searched and the years covered can be found in Appendix D in the full version of the original guideline document.

This is a clinical area that presented challenges when searching for the evidence. There was no clear population for each question, as well as a lack of consistency in the terminology used in the papers and in the application of index terms in the databases. These factors tend to lead to very large searches with imprecise retrieval. There was a need to balance this with the resources available to sift through large retrievals within the time allotted. For this reason there was extra reliance on finding evidence through methods such as checking reference lists or asking the GDG for known studies, as a supplement to the literature searches. This is in line with methodology suggested by the Cochrane Collaboration.

As an extra precaution, reviewers also checked through the all studies which were ordered but excluded for related reviews, to ensure that no relevant studies were missed. For example, when looking for studies for the volume and timing of resuscitation review, reviewers also checked the studies which had been ordered for the algorithm questions (there is a possibility that some algorithms effectively compare early vs. late resuscitation) and the fluid type question.

During the scoping stage, a search was conducted for guidelines and reports on the websites listed below and on organisations relevant to the topic. Searching for grey literature or unpublished literature was not undertaken. All references sent by stakeholders were considered.

- Guidelines International Network database ([www.g-i-n.net](http://www.g-i-n.net) )
- National Guideline Clearing House ([www.guideline.gov/](http://www.guideline.gov/) )
- National Institute for Health and Care Excellence (NICE) ([www.nice.org.uk](http://www.nice.org.uk) )
- National Institutes of Health Consensus Development Program ([consensus.nih.gov/](http://consensus.nih.gov/) )
- National Library for Health ([www.library.nhs.uk/](http://www.library.nhs.uk/) )

#### Health Economic Literature Search

Systematic literature searches were also undertaken to identify health economic evidence within published literature relevant to the review questions. The evidence was identified by conducting broad searches relating to specific key areas in the NHS economic evaluation database (NHS EED), the Health Economic Evaluations Database (HEED) and health technology assessment (HTA) databases with no date restrictions. Additionally, the searches were run on MEDLINE and EMBASE, with a specific economic filter to ensure publications that had not yet been indexed by these databases were identified. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English language.

The search strategies for health economics are included in Appendix D in the full version of the original guideline document. All searches were updated on 12 March 2013. No papers published after this date were considered.

#### Evidence of Effectiveness

##### The Research Fellow:

- Identified potentially relevant studies for each review question from the relevant search results by reviewing titles and abstracts – full papers were then obtained.
- Reviewed full papers against pre-specified inclusion/exclusion criteria to identify studies that addressed the review question in the appropriate population and reported on outcomes of interest (see review protocols in Appendix C in the full version of the original guideline document).

##### Inclusion/Exclusion

Evidence was searched and assessed according to the review protocols for each clinical question formed. See the review protocols in Appendix C in the full version of the original guideline document for full details.

A major consideration in determining the inclusion and exclusion criteria in the protocol was the applicability of the evidence to the guideline population. The population within the scope of the guideline is hospitalised adults, with the exclusion of certain populations from the scope and this is broadly adhered to in most reviews. However, the GDG discussed and decided upon additional inclusion or exclusion criteria for each protocol according to the clinical context of the review question. In areas where evidence was anticipated to be lacking, decisions were made to consider populations or settings not included within this guideline if the GDG considered the evidence as indirectly applicable. Some examples of how this

was applied include:

- Patients who had major cardiac surgery were excluded in intravenous (IV) fluid intervention reviews on types and volumes of fluid, but included in the assessment of weight monitoring.
- Studies of resuscitation conducted in the intensive care unit (ICU) setting were included in the resuscitation review.
- The search for evidence for fluid replacement included patients with diabetes mellitus.

More information about "Indirectness" is available in section 3.3.7 in the full version of the original guideline document.

Laboratory studies were excluded because the populations used (healthy volunteers, animals or in vitro) and settings are artificial and not comparable to the population we are making recommendations for. These studies would undoubtedly be of very low quality as assessed by GRADE and therefore randomized controlled trials (RCTs), cohort studies or GDG consensus opinion was considered preferable.

Literature reviews, letters and editorials, foreign language publications and unpublished studies were excluded.

## Number of Source Documents

Not stated

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate
Very Low	Any estimate of effect is very uncertain

## Methods Used to Analyze the Evidence

Meta-Analysis of Randomized Controlled Trials

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

### Evidence of Effectiveness

The Research Fellow:

- Critically appraised relevant studies using the appropriate checklist as specified in The Guidelines Manual.
- Extracted key information about the study's methods and results into evidence tables (see evidence tables included in Appendix E in the full version of the original guideline document).

- Generated summaries of the evidence by outcome (included in the relevant chapter write-ups in the full version of the original guideline document):
  - Randomised studies: meta analysed, where appropriate and reported in Grading of Recommendations Assessment, Development, and Evaluation (GRADE) profiles (for clinical studies)
  - Observational studies: data presented as a range of values in GRADE profiles
  - Qualitative studies: each study summarised in a table where possible, otherwise presented in a narrative.

## Methods of Combining Clinical Studies

### *Data Synthesis for Intervention Reviews*

Where possible, meta-analyses were conducted to combine the results of studies for each review question using Cochrane Review Manager (RevMan5) software. Fixed-effects (Mantel-Haenszel) techniques were used to calculate risk ratios (relative risk) for the binary outcomes. The continuous outcomes were analysed using an inverse variance method for pooling weighted mean differences and where the studies had different scales, standardised mean differences were used.

Statistical heterogeneity was assessed by considering the chi-squared test for significance at  $p < 0.1$  or an I-squared inconsistency statistic of  $> 50\%$  to indicate significant heterogeneity. Where there was heterogeneity and a sufficient number of studies, sensitivity analyses were conducted based on risk of bias and pre-specified subgroup analyses were carried out as defined in the protocol. Assessments of potential differences in effect between subgroups were based on the chi-squared tests for heterogeneity statistics between subgroups. If no sensitivity analysis was found to completely resolve statistical heterogeneity then a random effects (DerSimonian and Laird) model was employed to provide a more conservative estimate of the effect.

The means and standard deviations of continuous outcomes were required for meta-analysis. However, in cases where standard deviations were not reported, the standard error was calculated if the p-values or 95% confidence intervals were reported and meta-analysis was undertaken with the mean difference and standard error using the generic inverse variance method in Cochrane Review Manager (RevMan5) software. Where p values were reported as "less than", a conservative approach was undertaken. For example, if p value was reported as " $p < 0.001$ ", the calculations for standard deviations were based on a p value of 0.001. If these statistical measures were not available then the methods described in section 16.1.3 of the Cochrane Handbook 'Missing standard deviations' were applied as the last resort.

For binary outcomes, absolute differences in event rates were also calculated using the GRADEpro software using total event rate in the control arm of the pooled results and presented in the "Clinical Summary of Findings Table" in the full version of the original guideline document.

Pre-specified subgroup analyses were conducted for populations of interest. These are groups where it had been identified that the interventions were likely to have different effect (effect modifiers), rather than prognostic factors. Although prognostic factors are usually not good candidates for subgrouping in meta-analysis, it is often impossible to completely predict whether a potential difference in effect is due to a difference in how the intervention may work in a group, or in how it will affect all outcomes; for example active cancer is a prognostic factor, but can also possibly affect how anticoagulants work. When such subgroups are identified, studies were sub grouped to observe whether there might be differences in effects between different groups of patients.

## Appraising the Quality of Evidence by Outcomes

The evidence for outcomes from the included RCT and observational studies were evaluated and presented using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group (<http://www.gradeworkinggroup.org/> ). The software (GRADEpro) developed by the GRADE working group was used to assess the quality of each outcome, taking into account individual study quality and the meta-analysis results. The "Clinical evidence profile" tables presented summarise the quality of evidence and the findings of the reviews in the guideline. The tables present the pooled outcome data (where appropriate), an absolute measure of intervention effect and the summary of quality of evidence for that outcome. In these tables, the columns for intervention and control indicate the sum of the sample size for continuous outcomes. For binary outcomes such as number of patients with an adverse event, the event rates ( $n/N$ : number of patients with events divided by sum of number of patients) are shown with percentages. Reporting or publication bias was only taken into consideration in the quality assessment and included in the Clinical Study Characteristics table if it was apparent.

Each outcome was examined separately for the quality elements listed and defined in Table 2 and each graded using the quality levels listed in Table 3 in the full version of the original guideline document. The main criteria considered in the rating of these elements are discussed below (see section 3.3.4, Grading of Evidence, in the full version of the original guideline document). Footnotes were used to describe reasons for downgrading a quality element as having serious or very serious problems. The ratings for each component were summed to obtain an overall assessment for each outcome.

## Grading the Quality of Clinical Evidence

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using Grading of Recommendations, Assessment, Development and Evaluation (GRADE):

1. A quality rating was assigned, based on the study design. Randomised controlled trials (RCTs) start HIGH and observational studies as LOW, uncontrolled case series as LOW or VERY LOW.
2. The rating was then downgraded for the specified criteria: Study limitations, inconsistency, indirectness, imprecision and reporting bias. These criteria are detailed below. Observational studies were upgraded if there was: a large magnitude of effect, dose-response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have "serious" or "very serious" risk of bias was rated down -1 or -2 points respectively.
3. The downgraded/upgraded marks were then summed and the overall quality rating was revised. For example, all RCTs started as HIGH and the overall quality became MODERATE, LOW or VERY LOW if 1, 2 or 3 points were deducted respectively.
4. The reasons or criteria used for downgrading were specified in the footnotes.

See the full version of the original guideline document for details about study limitations, inconsistency, indirectness, and imprecision.

## Evidence Statements

Evidence statements were formed for each outcome indicating the quantity and quality of evidence available, and the outcome and population to which they relate. Where possible these were drafted for each subgroup or by outcome. An overall evidence summary for a particular intervention was presented, where possible.

## Undertaking New Health Economic Analysis

As well as reviewing the published economic literature for each review question new economic analysis was undertaken by the health economist in selected areas. Priority areas for new health economic analysis were agreed by the GDG after formation of the review questions and consideration of the available health economic evidence.

The GDG identified monitoring, fluid type for resuscitation and fluid type for maintenance as the highest priority areas for original economic modelling (see sections 6.3.1.3, 6.3.2.3 7.2.3.3, 7.3.2, 7.2.4.2 in the full version of the original guideline document).

In all three areas, the systematic review did not produce strong enough evidence to evaluate cost-effectiveness, so cost analyses were developed. The following general principles were adhered to:

- Methods were consistent with the NICE reference case, where possible.
- The GDG was involved in the design of the model, selection of inputs and interpretation of the results.
- When published data was not available GDG expert opinion was used to populate the model.
- Model inputs and assumptions were reported fully and transparently.
- The results were subject to sensitivity analysis and limitations were discussed.
- The model was peer-reviewed by another health economist at the NCGC.

Full methods for the cost analyses are described in Appendices L, M and N in the full version of the original guideline document.

## In the Absence of Economic Evidence

When no relevant published studies were found, and a new analysis was not prioritised, the GDG made a qualitative judgement about cost effectiveness by considering expected differences in resource use between options and relevant UK NHS unit costs alongside the results of the clinical review of effectiveness evidence.

## Methods Used to Formulate the Recommendations

### Expert Consensus

### Informal Consensus

## Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

A multidisciplinary Guideline Development Group (GDG) comprising professional group members and consumer representatives of the main stakeholders developed this guideline.

The group met every 5 to 6 weeks during the development of the guideline. Staff from the NCGC provided methodological support and guidance for the development process. The team working on the guideline included a project manager, systematic reviewers, health economists and information scientists. They undertook systematic searches of the literature, appraised the evidence, conducted meta-analysis and cost effectiveness analysis where appropriate and drafted the guideline in collaboration with the GDG.

### Developing Recommendations

Over the course of the guideline development process, the GDG was presented with:

- Evidence tables of the clinical and economic evidence reviewed from the literature. All evidence tables are in Appendix E (clinical evidence) and Appendix F (economic evidence) in the full version of the original guideline document.
- Summary of clinical and economic evidence and quality (as presented in chapters 5-10 in the full version of the original guideline document)
- Forest plots and summary ROC curves (see Appendix G in the full version of the original guideline document)
- A description of the methods and results of the cost-sensitivity analysis undertaken for the guideline (see Appendices L, M, N in the full version of the original guideline document)

Recommendations were drafted based on GDG interpretation of the available evidence, taking into account the balance of benefits and harms and evidence of cost effectiveness. When clinical and economic evidence was of poor quality, conflicting or absent, the GDG drafted recommendations based on expert opinion. The considerations for making consensus based recommendations included the balance between potential harms and benefits, economic or implications compared to the benefits, current practices, recommendations made in other relevant guidelines, patient preferences and equality issues. Consensus on recommendations was achieved through discussions in the GDG meetings. The GDG also considered areas where the uncertainty was sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation.

The main considerations specific to each recommendation are outlined in the Evidence to Recommendation Section preceding the recommendation section.

## Rating Scheme for the Strength of the Recommendations

### Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

#### Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

#### Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost-effective. Similar forms of words (for example, 'Do not offer...') are used when the GDG is confident that an intervention will not be of benefit for most patients.

#### Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost-effective, but other options may be similarly cost-effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and

discussing the options with the patient.

## Cost Analysis

### Cost-effectiveness Criteria

In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

- a. The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
- b. The intervention cost less than £20,000 per quality adjusted life year (QALY) gained compared with the next best strategy.

If the GDG recommended an intervention that was estimated to cost more than £20,000 per QALY gained, or did not recommend one that was estimated to cost less than £20,000 per QALY gained, the reasons for this decision are discussed explicitly in the 'from evidence to recommendations' section of the relevant chapter with reference to issues regarding the plausibility of the estimate or to the factors set out in the National Institute for Health and Care excellence (NICE) report 'Social value judgements: principles for the development of NICE guidance'. If a study reported the cost per life year gained but not QALYs, the cost per QALY gained was estimated by multiplying by an appropriate utility estimate to aid interpretation. The estimated cost per QALY gained is reported in the economic evidence profile with a footnote detailing the life-years gained and the utility value used. When QALYs or life years gained are not used in the analysis, results are difficult to interpret unless one strategy dominates the others with respect to every relevant health outcome and cost.

Reviews of the relevant published health economic literature identified in the literature search are presented alongside the clinical effectiveness reviews in the full version of the original guideline document (see the "Availability of Companion Documents" field). In addition, refer to Appendices L, M, and N in the full version of the original guideline document for cost sensitivity analyses of:

- Monitoring and assessment strategies for intravenous fluid therapy
- Types of intravenous fluids for resuscitation
- Intravenous fluids for routine maintenance

## Method of Guideline Validation

### External Peer Review

### Internal Peer Review

## Description of Method of Guideline Validation

The guidance is subject to a six week public consultation and feedback as part of the quality assurance and peer review the document. All comments received from registered stakeholders are responded to in turn and posted on the National Institute for Health and Care Excellence (NICE) website when the pre-publication check of the full guideline occurs.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

Appropriate management of intravenous (IV) fluid therapy for adults in the hospital setting to reduce morbidity and mortality and lead to better patient outcomes

## Potential Harms

Complications of intravenous (IV) fluid therapy, including hyponatraemia, volume overload, volume depletion and acute kidney injury (AKI)

## Qualifying Statements

### Qualifying Statements

- This guidance represents the view of the National Institute for Health and Care Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.
- Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If someone does not have the capacity to make decisions, healthcare professionals should follow the [Department of Health's advice on consent](#) , the [code of practice that accompanies the Mental Capacity Act](#)  and the supplementary [code of practice on deprivation of liberty safeguards](#) . In Wales, healthcare professionals should follow [advice on consent from the Welsh Government](#) .
- NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in [Patient experience in adult NHS services](#) .
- For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision.
- Health care providers need to use clinical judgement, knowledge and expertise when deciding whether it is appropriate to apply guidelines. The recommendations cited here are a guide and may not be appropriate for use in all situations. The decision to adopt any of the recommendations cited here must be made by the practitioners in light of individual patient circumstances, the wishes of the patient, clinical expertise and resources.

## Implementation of the Guideline

### Description of Implementation Strategy

The National Institute for Health and Care Excellence (NICE) has developed tools to help organisations implement this guidance. These are available on the [NICE Web site](#)  (see also the "Availability of Companion Documents" field).

#### Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

#### Principles and Protocols for Intravenous Fluid Therapy

- When prescribing intravenous (IV) fluids, remember the 5 Rs: Resuscitation, Routine maintenance, Replacement, Redistribution and

#### Reassessment.

- Offer IV fluid therapy as part of a protocol (see Algorithms for IV fluid therapy in the full version of the guideline document [see the "Availability of Companion Documents" field]):
  - Assess patients' fluid and electrolyte needs following Algorithm 1: Assessment.
  - If patients need IV fluids for fluid resuscitation, follow Algorithm 2: Fluid resuscitation.
  - If patients need IV fluids for routine maintenance, follow Algorithm 3: Routine maintenance.
  - If patients need IV fluids to address existing deficits or excesses, ongoing abnormal losses or abnormal fluid distribution, follow Algorithm 4: Replacement and redistribution.
- Patients should have an IV fluid management plan, which should include details of:
  - The fluid and electrolyte prescription over the next 24 hours
  - The assessment and monitoring plan.
  - Initially, the IV fluid management plan should be reviewed by an expert daily. IV fluid management plans for patients on longer-term IV fluid therapy whose condition is stable may be reviewed less frequently.

#### Assessment and Monitoring

- Assess the patient's likely fluid and electrolyte needs from their history, clinical examination, current medications, clinical monitoring and laboratory investigations:
  - History should include any previous limited intake, thirst, the quantity and composition of abnormal losses (see "Diagram of ongoing losses" in the original guideline document), and any comorbidities, including patients who are malnourished and at risk of refeeding syndrome.
  - Clinical examination should include an assessment of the patient's fluid status, including:
    - Pulse, blood pressure, capillary refill and jugular venous pressure
    - Presence of pulmonary or peripheral oedema
    - Presence of postural hypotension
  - Clinical monitoring should include current status and trends in:
    - National Early Warning Score (NEWS)
    - Fluid balance charts
    - Weight
  - Laboratory investigations should include current status and trends in:
    - Full blood count
    - Urea, creatinine and electrolytes
- All patients continuing to receive IV fluids need regular monitoring. This should initially include at least daily reassessments of clinical fluid status, laboratory values (urea, creatinine and electrolytes) and fluid balance charts, along with weight measurement twice weekly. Be aware that:
  - Patients receiving IV fluid therapy to address replacement or redistribution problems may need more frequent monitoring.
  - Additional monitoring of urinary sodium may be helpful in patients with high-volume gastrointestinal losses. (Reduced urinary sodium excretion [less than 30 mmol/l] may indicate total body sodium depletion even if plasma sodium levels are normal. Urinary sodium may also indicate the cause of hyponatraemia, and guide the achievement of a negative sodium balance in patients with oedema. However, urinary sodium values may be misleading in the presence of renal impairment or diuretic therapy.)
  - Patients on longer-term IV fluid therapy whose condition is stable may be monitored less frequently, although decisions to reduce monitoring frequency should be detailed in their IV fluid management plan.
- Clear incidents of fluid mismanagement (for example, unnecessarily prolonged dehydration or inadvertent fluid overload due to IV fluid therapy) should be reported through standard critical incident reporting to encourage improved training and practice (see "Consequences of fluid mismanagement to be reported as critical incidents" in the original guideline document).

#### Resuscitation

- If patients need IV fluid resuscitation, use crystalloids that contain sodium in the range 130–154 mmol/l, with a bolus of 500 ml over less than 15 minutes. (For more information, see the "Composition of commonly used crystalloids table" in the original guideline document.)

#### Routine Maintenance

- If patients need IV fluids for routine maintenance alone, restrict the initial prescription to:
  - 25–30 ml/kg/day of water and
  - Approximately 1 mmol/kg/day of potassium, sodium and chloride and

- Approximately 50–100 g/day of glucose to limit starvation ketosis. (This quantity will not address patients' nutritional needs; see the NICE guideline [Nutrition support in adults](#)  [NICE clinical guideline 32])

For more information see "IV fluid prescription for routine maintenance over a 24-hour period" in the original guideline document.

#### Training and Education

- Hospitals should establish systems to ensure that all healthcare professionals involved in prescribing and delivering IV fluid therapy are trained on the principles covered in this guideline, and are then formally assessed and reassessed at regular intervals to demonstrate competence in:
  - Understanding the physiology of fluid and electrolyte balance in patients with normal physiology and during illness
  - Assessing patients' fluid and electrolyte needs (the 5 Rs: Resuscitation, Routine maintenance, Replacement, Redistribution and Reassessment)
  - Assessing the risks, benefits and harms of IV fluids
  - Prescribing and administering IV fluids
  - Monitoring the patient response
  - Evaluating and documenting changes and
  - Taking appropriate action as required
- Hospitals should have an IV fluids lead, responsible for training, clinical governance, audit and review of IV fluid prescribing and patient outcomes.

## Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need

Getting Better

### IOM Domain

Effectiveness

Safety

## Identifying Information and Availability

### Bibliographic Source(s)

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2013 Dec

## Guideline Developer(s)

National Guideline Centre - National Government Agency [Non-U.S.]

## Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

## Guideline Committee

Guideline Development Group

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## Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Development Group (GDG) members declared interests including consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared arising conflicts of interest, which were also recorded in Appendix B in the full version of the guideline document (see the "Availability of Companion Documents" field).

Members were either required to withdraw completely or for part of the discussion if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Appendix B in the full version of the guideline document (see the "Availability of Companion Documents" field).

## Guideline Status

This is the current release of the guideline.

## Guideline Availability

Electronic copies: Available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) .

## Availability of Companion Documents

The following are available:

- Intravenous fluid therapy in adults in hospital. Full guideline. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Dec. 194 p. (Clinical guideline; no. 174). Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) .
- Intravenous fluid therapy in adults in hospital. Appendices. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Dec. 275 p. (Clinical guideline; no. 174). Electronic copies: Available in PDF from the [NICE Web site](#) .
- Intravenous fluid therapy in adults in hospital. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Dec. (Clinical guideline; no. 174). Electronic copies: Available from the [NICE Web site](#) .
- Intravenous fluid therapy in adults in hospital. Clinical audit tool. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Dec. (Clinical guideline; no. 174). Electronic copies: Available from the [NICE Web site](#) .
- Intravenous fluid therapy in adults in hospital. Costing statement. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Dec. 10 p. (Clinical guideline; no. 174). Electronic copies: Available from the [NICE Web site](#) .
- The guidelines manual 2012. London (UK): National Institute for Health and Care Excellence (NICE); 2012 Nov. Electronic copies: Available from the [NICE Web site](#) .

An online educational tool is available to registered users from the [NICE Web site](#) .

## Patient Resources

The following is available:

- Intravenous fluid therapy in adults in hospital. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Nov. (Clinical guideline; No. 174). Electronic copies: Available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) . Also available for download as a Kindle or EPUB ebook from the [NICE Web site](#) .

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